NMCP COVID-19 Literature Report #31: Tuesday, 21 July 2020

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Purpose: These reports are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic; they are biweekly, planned for Tuesdays and Fridays. Please feel free to reach out with questions and suggestions for future topics.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global 14,774,887 confirmed cases and 611,533 deaths in 188 countries/regions

*United States** top 5 states by cases (Virginia is ranked 15th)

	TOTAL US	NY	CA	FL	TX	NJ
Confirmed Cases	3,858,646	408,181	399,016	369,833	343,783	177,256
Tested	46,469,524	5,164,812	6,414,321	3,052,106	2,984,554	1,802,874
Recovered	NA	72,229	NA	NA	177,871	31,448
Deaths	141,426	32,519	7,776	5,205	4,106	15,737

*see census.gov for current US Population data; NA: not all data available JHU CSSE as of 1100 EDT 21 July 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	79,371	1,790	751	1,237	2,329	1,046	780	2,829
Hospitalized	7,267	174	43	64	145	101	76	154
Deaths	2,048	24	4	14	21	21	45	38

VA DOH as of 1100 EDT 21 July 2020

Changes to These Reports

Starting Friday, 24 July 2020, the NMCP COVID-19 literature report will be moving to once-a-week publication. The plan is for the website (https://nmcp.libguides.com/covidreport) to be updated throughout the week, and a report generated on Friday for distribution.

From the CDC

For Healthcare Professionals (HCPs)

CDC: Criteria for Return to Work for Healthcare Personnel with SARS-CoV-2 Infection (Interim Guidance; updated 17 July 2020)

Summary of changes:

- Except for rare situations, a test-based strategy is no longer recommended to determine when to allow HCP to return to work.
- For HCP with severe to critical illness or who are severely immunocompromised[1], the recommended duration for work exclusion was extended to 20 days after symptom onset (or, for asymptomatic severely immunocompromised[1] HCP, 20 days after their initial positive SARS-CoV-2 diagnostic test).
- Other symptom-based criteria were modified as follows:
    - Changed from "at least 72 hours" to "at least 24 hours" have passed since last fever without the use of fever-reducing medications
    - Changed from "improvement in respiratory symptoms" to "improvement in symptoms" to address expanding list of symptoms associated with COVID-19

Footnote 1: The studies used to inform this guidance did not clearly define “severely immunocompromised”. For the purposes of this guidance, CDC used the following definition that was created to more generally address HCP occupational exposures.

- Some conditions, such as being on chemotherapy for cancer, untreated HIV infection with CD4 T lymphocyte count < 200, combined primary immunodeficiency disorder, and receipt of prednisone >20mg/day for more than 14 days, may cause a higher degree of immunocompromise and require actions such as lengthening the duration of HCP work restrictions.
- Other factors, such as advanced age, diabetes mellitus, or end-stage renal disease, may pose a much lower degree of immunocompromise and not clearly affect occupational health actions to prevent disease transmission.
- Ultimately, the degree of immunocompromise for HCP is determined by the treating provider, and preventive actions are tailored to each individual and situation.

Selected Primary Literature

Recently published in peer-reviewed journals

JAMA: Thrombosis in Hospitalized Patients With COVID-19 in a New York City Health System (20 July 2020)

> "In patients with COVID-19 hospitalized in a large New York City health system, a thrombotic event occurred in 16.0%. D-dimer level at presentation was independently associated with thrombotic events, consistent with an early coagulopathy.
>
> Prior studies varied regarding the precise incidence of thrombosis; however, all suggested a heightened risk in patients with COVID-19. This analysis found variation by clinical setting and type of thrombosis event. While thrombosis is observed in other acute infections (eg, 5.9% prevalence during the 2009 influenza pandemic), the thrombotic risk appears higher in COVID-19. Thrombosis in patients with COVID-19 may be due to a cytokine storm, hypoxic injury, endothelial dysfunction, hypercoagulability, and/or increased platelet activity."

JAMA Netw Open: Completion of Advance Directives and Documented Care Preferences During the Coronavirus Disease 2019 (COVID-19) Pandemic (20 July 2020)

> "This study reveals a 4.9-fold increase in online AD [advance directive] completion as well as more comprehensive completion since the onset of the COVID-19 pandemic in the absence of contemporaneous efforts to increase uptake of the ACP [advance care planning] platform. Distributions of preferences were largely unchanged. Study limitations include unmeasured trends that may affect AD demand. Furthermore, while the platform is publicly available, it is largely used by patients within a single health system. The increased demand for AD documentation might be explained by an increased sense of AD importance owing to COVID-19–induced hospital visitation restrictions, calls for clinicians to promote ACP, or because COVID-19 has provided new motivation for patients who have long wanted to complete ADs but previously failed to do so."

Lancet: Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial (20 July 2020)

> "We report the results of the first clinical study of ChAdOx1 nCoV-19 (AZD1222). The vaccine was safe and tolerated, with reduced reactogenicity when paracetamol was used prophylactically for the first 24 h after vaccination. Reactogenicity was reduced after a second dose. Humoral responses to SARS-CoV-2 spike protein peaked by day 28 post prime and cellular responses were induced in all participants by day 14. Neutralising antibodies were induced in all participants after a second vaccine dose. After two doses, potent cellular and humoral immunogenicity was present in all participants studied.
>
> A vaccine against SARS-CoV-2 could be used to prevent infection, disease, and death in the global population, with high-risk populations such as hospital workers and older adults (eg,

≥65 years of age) prioritised to receive vaccination. The immune correlates of protection against SARS-CoV-2 have not yet been determined. Immunisation with ChAdOx1 nCoV-19 results in rapid induction of both humoral and cellular immune responses against SARS-CoV-2, with increased responses after a second dose. Further clinical studies, including in older adults, should be done with this vaccine."

Lancet: Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial (20 July 2020)

"This study provides more evidence for the immunogenicity and safety of the Ad5-vectored COVID-19 vaccine in a larger population. To assess the vaccine in a more diverse population, we removed the age cap for the recruitment of participants for this phase 2 trial. Older individuals (ie, aged ≥55 years), many of whom often have chronic illness, have a high risk of serious illness and death associated with SARS-CoV-2 infection; thus, they are an important target population for a COVID-19 vaccine. Our results suggest a single-dose immunisation schedule of Ad5-vectored COVID-19 vaccine at 5 × 1010 viral particles is an appropriate regimen for healthy adults. Compared with the younger population, we found older people to have a significantly lower immune response, but higher tolerability, to the Ad5-vectored COVID-19 vaccine. Therefore, an additional dose might be needed to induce a better immune response in the older population, and this will be evaluated in a phase 2b trial.

Evidence from this phase 2 study indicates the candidate Ad5-vectored COVID-19 vaccine has a good safety profile, with only mild, transient adverse events related to vaccination and no serious adverse events. Single-dose immunisation with the vaccine induced rapid onset of immune responses within 14 days and significant humoral and cellular immune responses within 28 days in the majority of the recipients. We are planning an international multicentre, randomised, double-blind, controlled phase 3 effectiveness trial to further evaluate the efficacy of the vaccine. We are in the midst of a global COVID-19 pandemic; thus, timely sharing of the results of clinical trials with candidate vaccines is critical."

NEJM: Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report (17 July 2020)

"In this controlled, open-label trial comparing a range of possible treatments in patients who were hospitalized with Covid-19, we randomly assigned patients to receive oral or intravenous dexamethasone (at a dose of 6 mg once daily) for up to 10 days or to receive usual care alone. The primary outcome was 28-day mortality. Here, we report the preliminary results of this comparison.

A total of 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. Overall, 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization (age-adjusted rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; P<0.001). The proportional and absolute

between-group differences in mortality varied considerably according to the level of respiratory support that the patients were receiving at the time of randomization. In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94) but not among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55).

In patients hospitalized with Covid-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support."

Sci Rep: SARS-CoV-2 failure to infect or replicate in mosquitoes: an extreme challenge (17 July 2020)

"This research addresses public speculation that SARS-CoV-2 might be transmitted by mosquitoes. The World Health Organization has stated "To date there has been no information nor evidence to suggest that the new coronavirus could be transmitted by mosquitoes". Here we provide the first experimental data to investigate the capacity of SARS-CoV-2 to infect and be transmitted by mosquitoes. Three widely distributed species of mosquito; *Aedes aegypti*, *Ae. albopictus* and *Culex quinquefasciatus*, representing the two most significant genera of arbovirus vectors that infect people, were tested. We demonstrate that even under extreme conditions, SARS-CoV-2 virus is unable to replicate in these mosquitoes and therefore cannot be transmitted to people even in the unlikely event that a mosquito fed upon a viremic host."

BMJ: The role of chest radiography in confirming covid-19 pneumonia (16 July 2020)

"What you need to know

- A normal chest radiograph does not exclude covid-19 pneumonia
- No single feature of covid-19 pneumonia on a chest radiograph is specific or diagnostic, but a combination of multifocal peripheral lung changes of ground glass opacity and/or consolidation, which are most commonly bilateral, may be present
- Diagnosis might be complicated as covid-19 pneumonia may or may not be visible on chest radiograph; consider other causes for patients' respiratory symptoms."

Emerg Infect Dis: Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020 (16 July 2020)

"We analyzed reports for 59,073 contacts of 5,706 coronavirus disease (COVID-19) index patients reported in South Korea during January 20–March 27, 2020. Of 10,592 household contacts, 11.8% had COVID-19. Of 48,481 nonhousehold contacts, 1.9% had COVID-19. Use

of personal protective measures and social distancing reduces the likelihood of transmission."

Nature: Reconstruction of the full transmission dynamics of COVID-19 in Wuhan (16 July 2020)

> "As countries in the world review interventions for containing the COVID-19 pandemic, important lessons can be drawn by studying the full transmission dynamics of SARS-CoV-2 in Wuhan, China, where vigorous non-pharmaceutical interventions have suppressed the local COVID-19 outbreak. Here, we use a modelling approach to reconstruct the full-spectrum dynamics of COVID-19 between January 1, 2020 and March 8, 2020 across five periods marked by events and interventions based on 32,583 laboratory-confirmed cases. Accounting for presymptomatic infectiousness, time-varying ascertainment rates, transmission rates and population movements, we identify two key features of the outbreak: high covertness and high transmissibility. We estimate 87% (lower bound 53%) of the infections before March 8 were unascertained, potentially including asymptomatic and mild-symptomatic cases; and a basic reproduction number R0 of 3.54 (95% credible interval [CrI]: 3.40-3.67) in the early outbreak, much higher than for SARS and MERS. We observe that multi-pronged interventions had considerable positive effects on controlling the outbreak, decreasing the reproduction number to 0.28 (0.23-0.33) and by projection reducing the total infections in Wuhan by 96.0% as of March 8. We furthermore explore the probability of resurgence following lifting of all interventions after 14 days of no ascertained infections, estimating it at 0.32 and 0.06 based on models with 87% and 53% unascertained infections, respectively, highlighting the risk posed by unascertained cases in changing intervention strategies. These results provide important implications for continuing surveillance and interventions to eventually contain COVID-19 outbreaks."

Preprints—not yet peer-reviewed papers

arXiv, bioRxiv, and medRxiv are preprint servers: "[T]hese are preliminary reports that have not been peer-reviewed. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

medRxiv: Symptom clusters in Covid19: A potential clinical prediction tool from the COVID Symptom study app (posted 16 July 2020)

> "As no one symptom can predict disease severity or the need for dedicated medical support in COVID-19, we asked if documenting symptom time series over the first few days informs outcome. Unsupervised time series clustering over symptom presentation was performed on data collected from a training dataset of completed cases enlisted early from the COVID Symptom Study Smartphone application, yielding six distinct symptom presentations. Clustering was validated on an independent replication dataset between May 1- May 28th, 2020. Using the first 5 days of symptom logging, the ROC-AUC of need for respiratory

support was 78.8%, substantially outperforming personal characteristics alone (ROC-AUC 69.5%). Such an approach could be used to monitor at-risk patients and predict medical resource requirements days before they are required."

The six clusters are as follows:

1. ('flu-like' with no fever): Headache, loss of smell, muscle pains, cough, sore throat, chest pain, no fever.
2. ('flu-like' with fever): Headache, loss of smell, cough, sore throat, hoarseness, fever, loss of appetite.
3. (gastrointestinal): Headache, loss of smell, loss of appetite, diarrhea, sore throat, chest pain, no cough.
4. (severe level one, fatigue): Headache, loss of smell, cough, fever, hoarseness, chest pain, fatigue.
5. (severe level two, confusion): Headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain.
6. (severe level three, abdominal and respiratory): Headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain, shortness of breath, diarrhea, abdominal pain.

Webinars and Calls

WHAT:	CDC Clinician Outreach and Communication Activity (COCA) Call
TOPIC:	Coronavirus Disease 2019 (COVID-19) and Diabetes: The Importance of Prevention, Management, and Support "During this COCA Call, presenters will focus on current information about the impact and increased risk for COVID-19 complications in people with diabetes and the importance of diabetes prevention, management, and support."
WHEN:	Tuesday, 28 July 2020 1400-1500 ET
DETAILS:	https://emergency.cdc.gov/coca/calls/2020/callinfo_072820.asp

News in Brief

Dr. Fauci warns that there is "no end in sight" for COVID-19 (Medpage).

As numerous states report record-breaking numbers of coronavirus cases, mainland China reports 11 new cases (Reuters).

The Army has over 7,000 coronavirus cases, and the military as a whole has over 21,000 positive tests; according to data from the Pentagon, the difference in infections between the Army and Navy is now 1,653 cases (Stripes).

A new COVID-19 relief bill has hit a snag over funding the CDC, testing and contact tracing, and vaccine support for Defense and others (WaPo).

COVID Data and the Government

Dozens of professional groups, associations, and organizations, including the Infectious Diseases Society of America, have signed a letter to the current administration urging it to reverse its decision to have coronavirus data bypass the CDC (IDSA).

The HHS unveiled its new COVID-19 dashboard on Monday, 20 July (HHS).

Research, Testing, Treatments, and Vaccines

NIH's "All of Us" research project will include looking at racial disparities with COVID-19 (KHN).

More than 100,000 Americans have signed up to be in coronavirus vaccine clinical trials (USA Today).

Even staunch vaccine supporters are increasingly hesitant of a potential coronavirus vaccine, because of the rush to develop one and distrust in the government and regulatory bodies (NYT).

Thanks, Coronavirus

A possible unexpected benefit of the pandemic and subsequent lockdowns: a dip in premature births (NYT; see also medRxiv, medRxiv).

When supply chains were impacted by the pandemic, the FDA relaxed requirements for label changes with ingredient substitutions -- and that's a problem for people with food allergies (WaPo).

"Blowing out candles is basically spitting on your friends' cake. Will we ever do it again?" (WaPo)

In case you were planning a trip to the Bahamas, sorry… Americans are banned (Newsweek).

No job is safe: Tower of London guards (also known as Beefeaters) may face cuts for the first time since their founding in 1485 by Henry VII (WaPo).

Long Reads & Explainers

“Can we stop the next pandemic before it happens?” (GQ)

“How to Understand COVID-19 Numbers” (ProPublica).

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